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ICHTHYOSIS UTERI.*

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The mucous membrane of the cavity of the uterus is covered by columnar epithelium, which presents different appearances in the corpus and in the cervix. The columnar epithelium is shorter in the body than in the cervix; the nuclei of the epithelium of the body generally lie in the center of the cells; in the cervix they are at the base of the cells. In stained specimens the whole of the protoplasm of the epithelium of the body stains; in the cervix only the protoplasm round the nucleus. Many cells of the mucous membrane of the cervix are so-called goblet cells, and secrete mucus. The cells on the surface of the body are ciliated, and the movement of the cilia is directed toward the os uteri and not toward the tubes, as was formerly believed. Normally, one row only of columnar epithelium covers the mucous membrane. Occasionally between the bases of the full-grown cells are observed small cells, which probably become superficial cells and take the place of the old cells as they are thrown off. All the varieties of epithelium described also cover the surface of benignant tumors which grow from the uterine walls into the uterine cavity, unless these tumors have grown to an enormous size or have undergone degeneration.

All deviations from the condition above described would be considered pathological if it were not necessary to exercise great care in the use of the term "pathological" in an organ in which so many histological processes must be considered normal, which in all other organs would be considered pathological. Absence of the epithelium, for example, on all other mucous membranes is justly termed abnormal; but in the uterus it is observed in the early days of the puerperium, which certainly can not be considered a pathological condition. In the puerperium the new epithelium is furnished by the epithelium of the uterine glands, which, according to my observations

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(1) made on specimens taken from the living puerpera, reaches the surface about the ninth day after delivery.

Absence of the epithelium is also observed in very rare cases of puerperal atrophy, some of which I have had the privilege to observe (3). In pyometra the whole mucous membrane of the uterus is sometimes replaced by granular tissue and all epithelium has perished. I do not mention pregnancy as an instance of the absence of the epithelium, because modern researches have proved that the syncytium of the chorionic villi is nothing but the former epithelium of the surface of the uterus. The epithelium is not to any considerable extent absent during menstruation. Recent researches (2) have proved this in spite of the old theories of menstruation.

Change in form of the epithelium is observed in cases of hydro-metra and hæmatometra, because the mucous surface of the epithelium is stretched and consequently flattened out. The same change of form may take place in extra-uterine pregnancy or in pregnancy in one horn of a double uterus, where the mucous membrane of the empty cavity is transformed into a decidua. In these cases the epithelium of the surface has been said by some authors to be absent altogether; but Gottschalk published a case of extra-uterine pregnancy where he could see the epithelium quite distinctly, although it was flattened out so much that it had the appearance of endothelium rather than of columnar epithelium. I can confirm his observation by one of my own, which I made on the decidua delivered out of the empty horn of a double uterus, one horn of which had been pregnant.

In all the conditions above enumerated there is never more than one layer of epithelial cells on the surface of the mucous membrane. A condition, however, exists where the cavity of the uterus is lined with stratified epithelium perfectly similar to the epithelial covering of the skin or the vagina.

This very remarkable observation was first mentioned by Gautier at the international medical convention at Geneva, and was first fully described by Zeller (4) in 1884 under the name of ichthyosis or psoriasis uteri. Zeller's paper has long been treated lightly—even with decided doubt as to its correctness—but it has gained a very great importance since cases of squamous epithelioma have been observed in the cavity of the uterus. According to generally accepted ideas on the formation of malignant growths, we could not expect to find in the uterine cavity any other kind of cancer than that composed of and originating from columnar epithelium. Since Piering (5), however, first published a case of cancrroid of the body of the uterus in 1887, the num-

ber of cases has so much increased that gynæcologists have had to attribute very grave importance to the occurrence of stratified epithelium on the mucous membrane of the uterus.

Before entering into the discussion of these rare observations, I wish to mention that the literature contains records of three different conditions under which stratified epithelium is observed at places where we expect to find the normal columnar epithelium of the cavity of the uterus. I possess specimens which show two of these conditions—one, inversion of the uterus; the other, cervical polypi extending into the vagina. In a case of chronic inversion of the uterus I made a small excision of the mucous membrane of the uterus, and to my astonishment found it covered with stratified epithelium. The basal cells of this were cylindrical; then came several layers of many-shaped cells, among them some prickle cells, and on top of them one or several layers of perfectly flat cells, all of which contained well-stained nuclei. There were only very few glands left below the stratified epithelium, but they were not dilated. During menstruation I made a second excision, and found that the uterus had not thrown off the stratified epithelium, but that there were small hæmorrhages underneath the epithelial covering, which in some places had broken small openings through the epithelial lining, and had thus been discharged.

I have also several specimens of cervical polypi, the lower apex of which had been lying in the vagina, and invariably this part of the polypi was covered with stratified epithelium, consisting again of one basal cylindrical row and several rows of multangular cells, the surface being formed by one or two layers of perfectly flat cells. Only the surface of the polypi was covered by this squamous epithelium; the glands and the surface of the pedicle of the polypus showed the normal high columnar epithelium peculiar to the cervix, as described above. Williams, in his *Harveian Lectures for 1886 on Cancer of the Uterus* (6), describes a case of cervical polypus the lower end of which was capped by the same pavement epithelium at its lower apex as in the cases mentioned above. But in his case the pavement epithelium had sent processes into the substance of the growth and into some of the glands. He therefore calls the case one of squamous epithelioma; but it seems to me that he has not given sufficient evidence for this diagnosis. Judging from this illustration (Plate XI), I should venture to disagree with him; an oblique section of the surface of the polypus may have caused a deceptive appearance of carcinomatous strings or cords.

Pavement epithelium has been observed by Zeller (4), Küstner (8), Ruge (7), and others on cervical polypi, and by Ruge (7) and Gebhard (2) in inversion of the uterus. Ruge (7) mentions cases of large procidentia of the uterus with deep tears and ectropium of the cervix in which he observed stratified epithelium in the lower part of the uterine cavity. This is not astonishing, as this condition is practically nothing but a partial inversion of the uterus.

In all of the conditions just described the mucous membrane of the uterus is in contact with the vagina or the vulva. We may speak of a sort of infection with pavement epithelium brought about by contact with organs covered with the same variety of epithelium. It is impossible at present to determine whether air may exercise some chemical influence, inducing metamorphosis of columnar into stratified epithelium. Veit calls this process "epidermidalization"; Zeller thinks it belongs to the condition described by him as "ichthyosis uteri."

The observations so far recorded are confirmed by all authors who have treated of this subject, but the condition described by Zeller as "ichthyosis uteri" has met with very great distrust regarding the cavity of the uterus in cases where neither inversion nor polypus existed. It is therefore necessary to consider Zeller's report a little more fully.

Zeller (4) has examined fifty-four cases of chronic endometritis, fifty-one of them in persons less than fifty years old. In all of these cases he found the surface of the mucous membrane of the uterine cavity covered partly or totally with stratified epithelium resembling that of the skin or vagina. The most superficial cells could be stained yellow by picric acid; generally they contained nuclei; in very rare cases they did not. The number of layers of flat cells was from one to four. Below this stratified epithelium he always found the glands increased in size and number. The stratified epithelium sometimes filled the mouth of the glands and covered their columnar epithelium. In all cases the stratified epithelium of the surface formed papillæ. In some cases Zeller repeated his observations several times on the same patient, and then he found that, for instance, the first and third observations revealed stratified epithelium, while the second and fourth showed the normal columnar epithelium. The best specimens were found in cases which had been treated for a long time with intra-uterine injections, cauterization, etc., and Zeller mentions especially that he obtained very good specimens a few days after intra-uterine injection of tincture of iodine.

The results thus stated by Zeller are in direct contradiction with my experience and that of all other microscopists. I have examined Zeller's paper very carefully and have tried to find out if there could be a misunderstanding or a mistake, but, barring unimportant contradictions in regard to the number of cases observed, and to the occurrence of prickle cells, I could discover no inconsistencies in his essay.

I have examined microscopically more than two hundred cases of uterine scrapings, but in only one of them I found the condition described by Zeller. I also found it in a case of cancer of the cervix when I examined the apparently normal mucous membrane of the body.

The latter case showed the stratified epithelium as a level covering of the cavity of the uterus; there were no processes of the epithelium penetrating into the subjacent tissue. I could discover no traces of uterine glands. I consider, therefore, this case as an instance of simple ichthyosis uteri, coexisting with cancer of the cervix. The other case which I observed was very interesting, and I wish to dwell upon it a little longer.

Mrs. T., sixty years old, had had several children. Menstruation had ceased about the fiftieth year. For some weeks she had noticed moderate hæmorrhages and a slight discharge. On examination, I found the patient anæmic and cachectic; the organs of circulation and nutrition were normal; the uterus was small, anteverted, the os closed; slight discharge of a bloody fluid; no pains. After dilatation I scraped out the uterus, but could only get very few and very small portions of tissue. On examining them, I found (Fig. 1) part of them were composed of nothing but a thick layer of stratified epithelium; another part contained deeper layers of the mucous membrane of the uterus, and even small particles of the muscular coat of the uterus. The deeper layer of the mucous membrane contained some sinuous glands, the epithelium of which was columnar, but in several places there was more than one row of columnar epithelium. In one place a string of stratified epithelium penetrated through the mucous membrane into the muscular coat of the uterus, and the epithelial cells were in immediate contact with the muscle cells. Consequently there could be no doubt that there was cancer of the cavity of the uterus which had penetrated into the muscular wall and which, contrary to the usual forms of cancer of the cavity of the uterus, originated in squamous epithelium, not in columnar epithelium. As the vaginal portion had a perfectly normal appearance, the possibility of a metastasis of a cancrroid of the portio was excluded. The cancrroid of the cavity must there-

fore have grown from a pavement epithelium newly formed on the mucous membrane of the cavity. As the specimens did not show this distinctly, I scraped the lower part of the cavity again a few days after the first scraping. Again I could remove only very little tissue, but fortunately this small particle contained the explanation I was



FIG. 1.—Cancer of the body. Case T.

looking for. In this particle (Fig. 2) I saw the mucous membrane of the cervix, distinctly recognizable by the epithelium of the numerous glands contained in the section; this epithelium consisted of the typical columnar cells described above. The surface of this mucous membrane was covered by a thick layer of stratified epithelium. The basal cells of it were cylindrical; the surface was formed by flat cells, and between these layers were eight to ten rows of many-shaped cells.

The nuclei of these cells, especially of the many-shaped cells, very frequently contained karyokinetic figures, but none of them presented irregular shapes. Between the many-shaped cells there were several irregular openings filled with blood cells. On careful examination and comparison of the basis of the epithelial layer, these openings

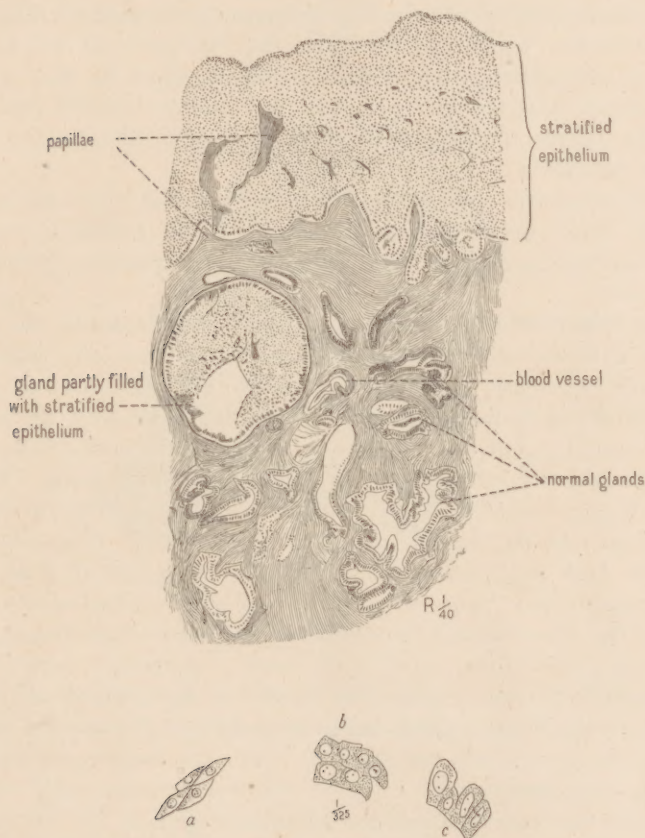


FIG. 2.—Ichthyosis uteri. Case T.

proved to be oblique sections through thin papillae with blood-vessels, which reached high up into the epithelial layers. A most remarkable feature was that a gland, immediately underlying the epithelium, was almost filled up with stratified epithelium on the side next to the surface. The resemblance of this picture with the histological appear-

ance of healing erosions is most striking. The other side of the gland showed cylindrical epithelium arranged sometimes in two or three rows. The borders of the gland were well defined. The other glands showed nothing abnormal. I believe that the resemblance of this specimen to one of Zeller's sketches, the normal condition of all glands but one, and the restriction of the stratified epithelium to one side of this gland, compel us to consider this specimen genuine ichthyosis. We are therefore entitled to the theory that the cavity of this uterus was lined throughout with stratified epithelium, which in some places was no longer confined to the surface, but had penetrated into the wall of the uterus, thus producing a real squamous epithelioma of the body of the uterus.

In the specimen which I have described first and which was taken from the cavity of the uterus with cancer of the cervix there were no traces of malignant growth originating from the squamous epithelium of the cavity.

If we follow Gebhard's definition (9) we must consider the two cases of ichthyosis which I have described to be essentially different. Gebhard's hypothesis is that there are two different series of cases with stratified epithelium: the one kind always remains limited to the surface—simple ichthyosis; the other kind has the tendency to penetrate into the subjacent tissue and form cancerous nests. Until now we have no possible means to discern these two different kinds if we do not see the terminal stages of the process. Pfannenstiel's definition (10) is therefore more valuable for practical purposes. Pfannenstiel says: "Not every case of stratified epithelium in the cavity of the uterus should be considered indicative of carcinoma, but the stratified epithelium, found in the cases of squamous epithelioma of the cavity of the uterus, must be considered the preliminary stage of the cancer, just as a glandular hypertrophy of the mucous membrane of the uterus, non-malignant in itself, can be the preliminary stage of adeno-carcinoma."

I would therefore lay down the following rules:

The clinical symptoms of ichthyosis are not sufficiently clear to enable us to found a diagnosis on them. Discharge and light hæmorrhage, the usual symptoms of ichthyosis, can as well be produced by cancer of the body and several other conditions as by ichthyosis.

If we scrape out a uterus and examine the scrapings microscopically, we may only find the stratified epithelium. We are then not enabled to give a diagnosis of cancer or of ichthyosis, but must reserve our diagnosis if the epithelium itself does not contain some further

clews as to the nature of the disease. In a case which I observed I found no layer below the epithelium; still, I was able to give the diagnosis of cancer, because in the middle of the stratified epithelium I discovered distinct cancerous pearls (Fig. 3). In other cases irregular karyokinetic figures may strengthen the suspicion of cancer so far as to justify hysterectomy. Pyometra has been observed in quite a considerable number of squamous epithelioma of the body of the uterus,

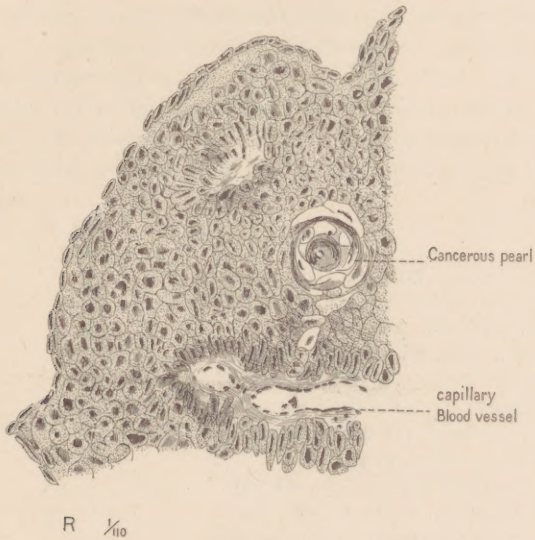


FIG. 3.

and this pathological condition in itself may render hysterectomy necessary if microscopical examination does not enable us to diagnose cancer.

In other cases the curette procures sufficient tissue for a precise diagnosis. If we find the stratified epithelium limited to the surface, or penetrating only into the mouth of the glands, the diagnosis must be ichthyosis. We must, however, always frequently observe these patients for some time, because we do not know if the ichthyosis will not undergo metamorphosis into cancer.

If, on the contrary, the microscope reveals cords of pavement epithelium penetrating into the tissues of the mucous membrane, or even into the muscular wall of the uterus, the diagnosis must be one of cancer, and speedy removal of the uterus is indicated.

Squamous epithelioma of the uterus does not necessarily originate in previous ichthyosis of the uterus, but squamous epithelioma of the cervix may spread over the mucous membrane of the body, as in cases described by Benckiser (11) and Hofmeier (12), or the cancrioid of the body may be a metastasis of a cancrioid of the cervix, as in a case described by Pfannenstiel (10).

To the cases originating in the cavity itself, as described by Piering (5), Gebhard (9), Löhlein (13), Fleischlen (14), Emanuel (15), I have added here the two cases described above. By the connection established by recent researches between cancrioid of the body and ichthyosis, the latter has gained an importance formerly unthought of. The subject deserves the full attention of the microscopist as well as the gynæcologist, and tends to show again that the latter can not do full justice to his specialty if he is not also a microscopist.

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RELiance BUILDING.

